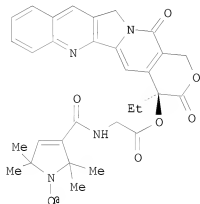


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L1 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2008:1297978 CAPLUS  
DOCUMENT NUMBER: 150:56371  
TITLE: First synthesis of novel spin-labeled derivatives of camptothecin as potential antineoplastic agents  
AUTHOR(S): Liu, Ying-Qian; Tian, Xuan; Yang, Liu; Zhan, Zong-Cheng  
CORPORATE SOURCE: School of Pharmacy, Lanzhou University, Lanzhou, 730000, Peop. Rep. China  
SOURCE: European Journal of Medicinal Chemistry (2008), 43(11), 2610-2614  
CODEN: EJMCAS; ISSN: 0223-5234  
PUBLISHER: Elsevier Masson SAS  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 150:56371  
GI



AB In an effort to improve the stability of labile lactone ring and water solubility of camptothecin, five novel spin-labeled camptothecin derivs. were synthesized by a simple modification of the carbodiimide method using the combination of scandium triflate (Sc(OTf)<sub>3</sub>) and 4-dimethylaminopyridine (DMAP), and the in vitro pharmacokinetic determination of the lactones of representative compound I showed that the biol. life span of their lactone forms in human and mouse plasma significantly increased when compared with their mother compound camptothecin. Also, the in vitro cytotoxicity of the compds. against human bladder cancer T-24 showed either similar or better activity than that of the parent drug, camptothecin, and clin. available drug, irinotecan.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:708475 CAPLUS  
DOCUMENT NUMBER: 143:326492  
TITLE: Radiosynthesis of carbon-11-labeled

camptothecin derivatives as potential positron emission tomography tracers for imaging of topoisomerase I in cancers

AUTHOR(S): Gao, Mingzhang; Miller, Kathy D.; Sledge, George W.; Zheng, Qi-Huang

CORPORATE SOURCE: Department of Radiology, Indiana University School of Medicine, Indianapolis, IN, 46202, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(17), 3865-3869  
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:326492

AB Four carbon-11-labeled camptothecin derivs., 9-[11C]methoxy-20(S)-camptothecin ([11C]5), 10-[11C]methoxy-20(S)-camptothecin ([11C]7), 9-nitro-10-[11C]methoxy-20(S)-camptothecin ([11C]9), and 9-[(11C)trimethylamino)methyl]-10-hydroxy-20(S)-camptothecin ([11C]11), have been synthesized as potential positron emission tomog. tracers for imaging of topoisomerase I in cancers.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:546425 CAPLUS

DOCUMENT NUMBER: 141:106651

TITLE: Preparation of isotope labeled camptothecin derivatives

INVENTOR(S): Giribone, Danilo; Forino, Romualdo; Barbugian, Natale; Fontana, Erminia

PATENT ASSIGNEE(S): Pharmacia Italia S.p.A., Italy

SOURCE: PCT Int. Appl., 75 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056398	A1	20040708	WO 2003-EP14801	20031219
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2509418	A1	20040708	CA 2003-2509418	20031219
AU 2003296720	A1	20040714	AU 2003-296720	20031219
EP 1578456	A1	20050928	EP 2003-813596	20031219
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003017434	A	20051116	BR 2003-17434	20031219
JP 2006510700	T	20060330	JP 2004-561428	20031219
MX 2005006746	A	20050908	MX 2005-6746	20050620

US 20060281776 A1 20061214 US 2006-540081 20060719  
PRIORITY APPLN. INFO.: EP 2002-80413 A 20021220  
WO 2003-EP14801 W 20031219  
OTHER SOURCE(S): CASREACT 141:106651; MARPAT 141:106651  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The present invention provides isotope labeled camptothecin analogs I [R1 = OH, R'; R2, R3, R4, R5, R6, R7, R8, R9 = 2H, H; X1, X2, X3, X4, X5, X6, X7, X8, X9 = 13C, C; Y = 15N, N; R10, R11, R12, R13, R14, R15, R16, R17, R18, R19, R20 = 2H, H; X10, X11, X12, X13, X14, X15, X16, X17, X18, X19, X20 = 13C, C; Y1, Y2 = 15N, N; with the proviso that at least one of C, H or N is an isotope], or their pharmaceutically acceptable salts, including irinotecan and SN-38, a process for their preparation and their use as internal stds. in anal. methods. Thus, labeled SN-38 II was prepared from 4-methoxyaniline via reaction with CD3CH2CN in PhMe, BC13 in CH2Cl2 and AlCl3 in ClCH2CH2Cl, followed by O-demethylation with HBr to give 2-H2N-5-HOC6H3COCH2CD3, which underwent cyclocondensation with pyranoindeoletrione III in PhMe containing AcOH and catalytic 4-MeC6H4SO3H. In addition, unlabeled SN-38 was acylated with 1-(chlorocarbonyl)-4-{{[15N]-piperidin-1-yl}piperidine or 1-(chlorocarbonyl)-4-(decadeuteriopiperidin-1-yl)piperidine.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1996:468534 CAPLUS

DOCUMENT NUMBER: 125:157685

ORIGINAL REFERENCE NO.: 125:29203a,29206a

TITLE: Stabilities of 3H- and 2H-labeled camptothecins

AUTHOR(S): Hinz, Hellmuth R.; Harris, Nicholas J.; Giovannella, Beppino C.; Ezell, Edward L.; Liehr, Joachim G.

CORPORATE SOURCE: Stehlin Foundation for Cancer Research, St. Joseph Hospital, Houston, TX, 77003, USA

SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (1996), 38(8), 733-742  
CODEN: JLCRD4; ISSN: 0362-4803

PUBLISHER: Wiley

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Com. available [3H]-camptothecin, labeled mainly at the C-5 position, had partially lost the tritium label after recovery from the plasma of a patient injected with this drug or after incubation in plasma at 38° for 72 h. Camptothecin dissolved in CH3O2H/2H2O, incorporated deuterium at the C-5 position with a 50% uptake after one day at pH 11.0 or after 10-11 days at pH 7.4. At pH 2.0, the deuterium uptake was negligible. Camptothecin, dissolved in deuterated sulfuric acid, incorporated 37 or 80% deuterium at C-14 when heated to 65 or 80°, resp. Com. available [3H]-camptothecin, labeled mainly at the C-5 position, is thus not useful for in vivo metabolism or pharmacokinetic studies due to rapid loss of tritium in plasma. In contrast, [3H]-camptothecin prepared as described in this paper for [2H]-camptothecin is expected to be useful.

L1 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:658715 CAPLUS  
DOCUMENT NUMBER: 123:74360  
ORIGINAL REFERENCE NO.: 123:12931a,12934a  
TITLE: Antitumor activities of a new indolocarbazole substance, NB-506, and establishment of NB-506-resistant cell lines, SBC-3/NB

AUTHOR(S): Kanzawa, Fumihiko; Nishio, Kazuto; Kubota, Naohiro; Saijo, Nagahiro

CORPORATE SOURCE: Pharmacology Division, National Cancer Center Res. Inst., Tokyo, 104, Japan

SOURCE: Cancer Research (1995), 55(13), 2806-13  
CODEN: CNREAB; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel anticancer glucosyl derivative of indolo-carbazole (NB-506), an inhibitor of DNA topoisomerase I, exhibited strong in vitro cytotoxicity against various human cancer cell lines. In order to elucidate its cytotoxic mechanisms, we established nine NB-506-resistant sublines. Among them, SBC-3/NB#9 was 454 time more resistant to NB-506 than the parent cell line. The SBC-3/NB#9 cells showed cross-resistance only to topoisomerase I inhibitors, such as 11.7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxy-camptothecin and 7-ethyl-10-hydroxy-camptothecin, and not to other anticancer drugs, such as vincristine, vinorelbine, vinblastine, Adriamycin, etoposide, and teniposide. These results indicate that the difference on the effect of topoisomerase I was considered to be related to a resistance mechanism. The topoisomerase I activities of nuclear exts. eluted from SBC-3/NB9 cells was only one-tenth of the parent cell activity. A Western blotting study indicated that this lower activity was due to a lower amount of DNA topoisomerase I. Furthermore, we found correlations between topoisomerase I activity and sensitivity to NB-506 in sublines with different degrees of resistance. Accumulation of 3H-labeled NB-506 by SB-3/NB#9 cells was only one-fifth of that by the parent cells, whereas intracellular accumulation of 3H-labeled camptothecin by both cell lines did not differ. The reduction of accumulation was specific to NB-506, and this result may explain why the resistance ratio for NB-506 was higher than those for 11.7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxy-camptothecin and 7-ethyl-10-hydroxy-camptothecin.

## L1 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1984:530954 CAPLUS  
DOCUMENT NUMBER: 101:130954  
ORIGINAL REFERENCE NO.: 101:19931a,19934a  
TITLE: Preparation of tritium-labeled camptothecin, 10-hydroxycamptothecin and nevidensin

AUTHOR(S): Zhang, Xin; Ding, Ruiqin

CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai, Peop. Rep. China

SOURCE: Hejishu (1984), (2), 47-8  
CODEN: NUTEDL; ISSN: 0253-3219

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

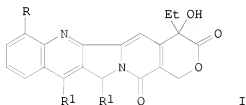
AB Title compds. were prepared by treating camptothecin, 10-hydroxycamptothecin, and nevidensin with CF3CO2H/T2O, Me2SO/T2, and CH3CO2H/T2O, resp.

## L1 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1981:498106 CAPLUS

10/540,081

DOCUMENT NUMBER: 95:98106  
ORIGINAL REFERENCE NO.: 95:16499a,16502a  
TITLE: The preparation of tritium- and deuterium-labeled camptothecin  
AUTHOR(S): Ronman, Peter E.; Wani, Mansukh C.; Wall, Monroe E.  
CORPORATE SOURCE: Research Triangle Inst., Research Triangle Park, NC, 27709, USA  
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1981), 18(3), 319-29  
CODEN: JLCRD4; ISSN: 0362-4803  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 95:98106  
GI



AB The labeled camptothecins I (R = T, R1 = H; R = H, R1 = D) were prepared from I (R = R1 = H) (II). Thus, II was nitrated, hydrogenated, and brominated to give I (R = Br, R1 = H) which was reduced by T2(g) in the presence of Pd/C to give I (R = T, R1 = H) with a sp. activity of 29 Ci/mol and a radiochem. purity of >95%. Reduction of d-II with D2(g) in the presence of Pd/C for 24 h gave optically active I (R = H, R1 = D).

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FILE 'CAPLUS' ENTERED AT 10:17:23 ON 30 APR 2009

L1 7 S LABELLED CAMPTOTHECIN OR LABELED CAMPTOTHECIN?

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